Association of ABO Blood Groups in Relation to Oral Cavity Cancers in Western Rajasthan

Shikha Saxena[1], Kamal Kant Gupta[2], Pragati Meena[3]

ABSTRACT

Introduction: Many previous studies found that the ABO blood type alters the individual susceptibility of some malignancies. The goal of this retrospective study was to evaluate the association between the type of ABO blood group and oral cavity cancers.

Material and Methods: The study was conducted in the Department of Physiology in collaboration with Department of Radiotherapy at Mathura Das Mathur Hospital of Dr. Sampurnanand Medical College, Jodhpur (Rajasthan), on 171 clinically diagnosed oral cavity cancer patients out of which 131 were males and 40 were females. The study period was from September 2006 to March 2008. The study was approved by the ethical committee of Dr S N Medical College, Jodhpur under Rajasthan University of Health Science Jaipur. The standard agglutination test was used to determine the ABO blood groups in oral cavity cancers patients. The statistical association of ABO blood groups and risk of oral cavity cancers was found out with Odd Ratios (OR).

Results: Oral cavity cancer cases (66 out of 171) were found in blood group A individuals (OR=6.54) followed by blood type O (OR= 4.3), B (OR= 3.18) in reference to blood type AB (OR=1). The male cancer patients were found to be higher incidence to develop oral cancers (76.00%) in comparison to females (23.39%).

Conclusion: Blood group A having maximum association with oral cavity cancers, followed by O, B and least preponderance related to blood group AB. Maximum oral cavity cancers was found in males in comparison with females.

Keywords: Oral cancers, Palate cancer and ABO blood group, Tongue cancer

INTRODUCTION

Cancer is characterized by abnormal growth of cells which have the ability to invade the adjacent tissues and sometimes even distant organs.[1] The term "oral cancer" includes a diverse group of tumors arising from the oral cavity.[2] Although oral cancer is rare and attracts little attention but it is more common than Hohgkins disease tumors of brain, liver, bone, thyroid gland, stomach, ovaries or cancer of cervix; its rank 12th among all cancers.[3]

In India, oral cancer accounts for about 40% of all cancers of the body and is a major public health problem with sufficient morbidity and mortality, emerging as a killer disease.[4] Oral cancer has multifactorial etiology and is significantly associated with risk factors of the individual's lifestyle, particularly, chronic use of tobacco, spicy food, alcohol and smoking. Many studies have indicated that genetic factors also have an influence on the etiology of cancer as the genes have been implicated in development and progression of oral cancer. Some studies reported that p53 gene has been found to be mutated in majority of oral cancer patients.[5]

Other possible factors in the development of oral cancer such as viral infections and different expression of ABO blood group antigens are also being studied.[6]

The mechanisms hypothesized behind the association between blood group A and carcinomas is that the carcinoma cells produce an antigen immunologically related to blood group A which particularly in O individuals may have a protective effect by preventing the growth and spread of the tumor. Because of this similarity, antibodies to A probably also attack precancerous and cancerous cells expressing this antigen. The homotypic and heterotypic cell adhesion mediated by interactions of certain blood group carbohydrates with corresponding lectins is a critically important event at the extravasations step of the metastatic cascade when metastatic cancer cells escape from circulation into distant sites of secondary tumor growth. People with blood groups A and AB lack antibodies to A and so are more prone to develop these carcinomas. The authors also propose that there is a small association between blood type A and cancer development. Type A individuals appear to be at a moderately increased risk for many cancers. Deletion or reduction of histo-blood group A or B antigen in tumors of A or B individuals is correlated with the degree of malignancy and metastatic potential in many types of human cancers.[7]

It is important to diagnose oral cancer in its early stages, since the management of small and localized tumors involves less morbidity and mortality than more advanced-stage disease, where treatment must be more aggressive. Indeed, the stage in which the disease is diagnosed is directly correlated to long-term survival.[8]

The present study was an attempt to correlate ABO blood groups frequency and to assess the utility of ABO blood group in relation to oral cavity cancers as a preclinical tumor marker. Thus, the objectives of this study were to document ABO blood group of patients suffering from malignancies of different oral cavity organs and to describe the association of malignancy with ABO blood group in Western Rajasthan.

MATERIAL AND METHODS

This was a retrospective hospital based study conducted in Mathura Das Mathur Hospital in Jodhpur, Rajasthan from September 2006 to March 2008. A total of 171 consecutive confirmed diagnosed oral cavity cancer patients were enrolled

[1]Ph D Scholar, Department of Physiology, S.M.S. Medical College, [2]Senior Resident, Department of General Surgery, Narayana Hirdayalaya Hospital, [3]Assistant Professor, Department of Obs and Gynae, NIMS Medical College, Jaipur, Rajasthan, India

Corresponding author: Shikha Saxena, 54 B, Ganguwal Park, Moti Dungri road, Jaipur, Rajasthan, India

How to cite this article: Shikha Saxena, Kamal Kant Gupta, Pragati Meena. Association of ABO blood groups in relation to oral cavity cancers in western rajasthan. International Journal of Contemporary Medical Research 2016;3(9):2661-2664.

in this study as patient group out of which 131 were males and 40 were females. The study was approved by Ethical Committee and Institutional Review Board of Dr. Sampurnanand Medical College, Jodhpur under Rajasthan University of Health Science, Jaipur. A written informed conscious consent was obtained from all subjects before their participation. The data of age, sex, ABO blood group and pathological status of cancer were collected from the Radiotherapy Department of Mathura Das Mathur Hospital, Jodhpur.

Inclusion criteria: Pathologically confirmed diagnosis of oral cavity cancers, laboratory data available for ABO blood type and detailed record of disease, course and history

Exclusion criteria: Familial cancer history, dietary habits, drinking alcohol had been taken.

Initially all patients completed a detailed questionnaire regarding their diet and habits, thorough history, detailed physical examinations and performed routine radiological and laboratory investigations including complete blood count (CBC) and tumor markers for oral cavity cancers. Blood samples were obtained via vacuum glass tubes containing EDTA. ABO blood tying was carried out with standard agglutination method. ABO blood groups were determined by using antiserum A and Antiserum B.

Standard Agglutination Method: In agglutination test firstly we prepared red cell suspension in a test tube and then in under aseptic precautions added a drop of blood. Then a drop of each antiserum (antiserum A, antiserum B) was placed on glass slide with the help of dropper and a drop of isotonic saline (used as control) was also placed on the slide. The slide was accordingly labeled as anti- A, anti- B and control. After 10 minutes, they were examined for the presence of agglutination (clumping of RBC) under low power microscope.[9]

Sample size determination: The sample size was determined by using the formula,[10] for comparing the difference of means between the groups with $\alpha = 0.05$, power = 80% and es = 0.30.

es = largest difference between any two groups to be detected / expected within the group

Standard Deviation es =diff / SD; Sample size = 171.

STATISTICAL ANALYSIS

For each factor, we calculated the adjusted Odds Ratios (OR) using maximum likelihood estimation.

RESULTS

Figure-1 shows that in distribution of all diagnosed 171 oral cavity cancers the maximum cases were of tongue, (41%) followed by tonsil cancers (21%). Least cancer cases were related to G L Sulcus (7%), pyriform fossae (5%), cheek (5%), and palate (2%).

Table-1 shows that in gender wise distribution of oral cancer cases, maximum preponderance was found in male (76.60%) gender in comparison with female (23.39%). Table-2 shows association of ABO blood group with different types of oral cavity cancers. In overall cancer a total of 171 cases, maximum cancer were found in blood group A (6.54), followed by O (4.3), B (3.18) and AB (1). In 171 oral cancer cases, in reference to blood group AB [OR 1], blood group A having 6.54 times higher association with cancers followed by blood group O [OR 4.3] and B [OR 3.18]. Out of 71 tongue cancer cases with reference to blood type AB (OR - 1), maximum cases were found in blood type A (n=26; OR= 4.55), followed by O (OR =2.88) and blood type B (OR= 2.48). Blood type A and O having OR 18.82 and 8.5 respectively, having higher risk for developing tonsil cancers with reference to AB blood group (OR 1), 35 buccal muccosa cancer cases were found and with reference to blood type AB (OR 1), preponderance of buccal mucosal cancer were found in blood type O (OR 3.55) followed by blood type A and B which

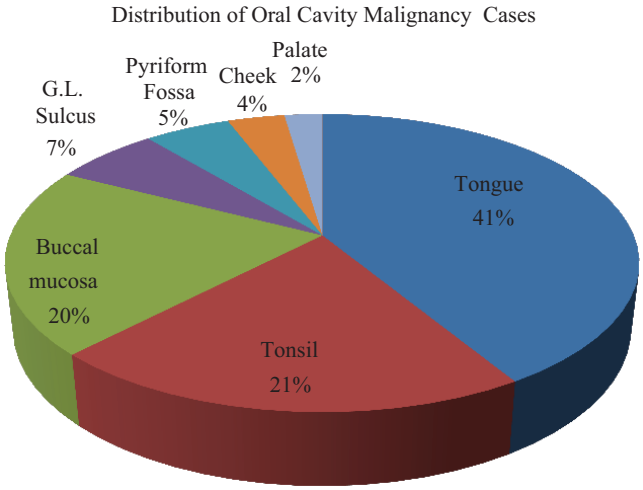

Figure-1: Distribution of cancer cases in relation to different oral cavity cancers.

Sex	No. of patients	Percentage
male	131	76.60%
female	40	23.39%

Table-1: Distribution of oral cancer cases in relation to sex.

S. No	Type of GIT Malignancy	No. Of Cases	Cases in Blood Groups							
			A		B		O		AB	
			No	*OR	No	*OR	No	*OR	No	*OR
1	Tongue	71	26	4.55	17	2.48	19	2.88	8	1 (R) **
2	Tonsil	36	14	18.82	8	4.86	12	8.5	2	1 (R) **
3	Buccal mucossa	35	10	2.4	7	1.5	13	3.55	5	1 (R) **
4	G.L. Sulcus	11	6	5.4	2	1 (R) **	3	1.69	-	-
5	Pyriform fossa	9	4	2.8	3	1.75	2	1 (R) **	-	-
6	Cheek	6	3	5	2	2.5	1	1 (R) **	-	-
7	Palate	4	3	9	1	1 (R) **	-	-	-	-
	Total	171	66	6.54	40	3.18	50	4.3	15	1 (R)

*OR=ODD's Ratio, **(R)=Reference OR

Table-2: Association of oral cavity malignancy with ABO blood group

having risk of 2.4 and 1.5 times respectively, for developing cancer. G L Sulcus, pyriform fossa, cheek and palate cancer cases were maximum related to blood type A (OR 5.4, 2.8, 5, 9) respectively.

DISCUSSION

Our study also showed that blood type A was more associated to oral cavity cancers and blood type AB having least association of risk of oral cavity cancers.

Blood has had a mysterious fascination for man since the dawn of time. A and B antigens are saccharide groups of glycoproteins present on RBC membrane. These antigens are not shared by all the members of the particular species and are called "iso-antigens". The alleles which determine the presence or absence of these antigens are called as "iso-alleles". Based on the presence of these blood group antigens, individuals may be categorized to belong to one of the four blood group A, B, AB and O.[4] Biochemical and molecular genetic studies have contributed to our molecular knowledge of blood group-associated molecules in the past few years.[11-14] Antigens defined by carbohydrate structures, among which ABO, Hh, Lewis and Secretor are the main representative species, are indirect gene products.[15] They are synthesized by Golgi-resident glycosyltransferases, which are the direct products of the blood group genes.

ABO antigens: ABO blood group antigens were initially identified as erythrocyte substances with a significance mainly ascribed to serology, it soon became clear that these antigens were found on most epithelial cells and in secretions.[16] These ABH antigens are carbohydrate antigens which in epithelia are expressed in a highly regulated way that correlates with the pattern of epithelial differentiation and with cell maturation.[17]

Some researchers have studied the relationship between ABO blood groups and oral cancer. The possibility of association between ABO blood groups and malignancy was first explored by Alexander.[18] Following a long gap thereafter; a study,[19] reported a close association between gastric cancer and blood group A. In India, studies done by Tyagi et al,[20] Mittal and Gupta,[21] Nayak,[22] and Baruah and Gogoi,[23] have shown that individuals with blood group A have predisposition for oral cancer. Raghavan[24] who studied the incidence of ABO blood groups in oral cancer cases of South Kanara district of India, found increased susceptibility of oral cancer among people with blood group A.

The immunehistochemical evaluations of oral squamous cell carcinoma have reported a loss of expression A and B in more than 80% of cases. These finding were also shown in potentially malignant lesions with epithelial dysplasia.[25]

Many malignant cells (such as those found in breast and stomach cancer) develop a tumor marker called Thomsen- Friedenrich (T) antigen, which is suppressed in normal healthy cells, Tn antigen (precursor of T antigen) only becomes unsuppressed as a cell become malignant. T and Tn antigens show some structural similarity to A antigen.[26] Blood group A individuals have the least aggressive antibody immune response against the T and Tn antigens and they are actually immunologically considered similar because of their shared terminal sugar (N-acetylgalactosamine), and so might be readily confused by immune system of blood group A individuals. Blood group A cancer patients had the greatest and most uniform suppression of the level of Tn antigens, irrespective of age, cancer stage, or tumor morphology and lower level of anti-B-isohemagglutinnins. This is probably at least a part of the explanation for the poorer outcomes in many cancers among blood group A individuals.[27]

The reason that deletion or reduction of the A or AB antigens in tumors of A or B individuals correlate with malignancy and metastatic potential may be due to lack of adhesiveness that a cancer cell achieves when it losses blood group antigens. The loss of blood antigens result in the tumor cells gaining the ability to move and circulate through the body, because blood type antigens loss the ability to express many of cell adhesion proteins, such as integrins, which normally express an A like antigen on their receptor and control cell movement. Blood Group “A” individuals have a very low immunologic response to T and Tn antigens because they share the same sugar (N-acetygalactosamine). This allows the cancer cells to bypass the immune system and replicate with little interference from the type A antibodies.[28]

Limitations: Because of resource constrain, small sample size and short time duration for the present study, the another view that the identification of genetic and environmental factors among racial and ethnic groups should offer some insights into the observed epidemiological data and advance opportunities to better understand the control and development of cancer. Collectively, we could hypothesize that tumors have more chance to thrive and maximum found in blood group A patients than those in other blood group.

CONCLUSION

In conclusion, it appears that different blood groups are associated with different manifestations of the disease. Blood group A apparently increases the risk for cancer. Different oral cavity cancers have the strongest association with blood type A group. But the racial and ethnic distribution of blood groups and size of sample is an important factor for predicting the cancer risk. Blood type needs to be considered together with other risk factors to understand the individual patient’s risk. The identification of genetic and environmental factors among racial and ethnic groups should offer some insights into the observed epidemiological data and advance opportunities to better understand the control and development of cancer.

ACKNOWLEDGEMENT

I sincerely thanks to Dr Jayant (Prof.), Dr N D Soni (Prof.and Head), Dept. of Physiology, Dr Pradeep Gaur (Prof.) Dept. of Radiotherapy, Dr S N Medical College, Jodhpur, Rajasthan and to all my colleagues and all the patients who help me in my work.

REFERENCES

1. Park K. Epidemiology of Communicable diseases. In: Park's text book of Preventive and Social Medicine. 15th ed. Jabalpur, India: Banarasidas Bhanot Publishers. 1997. p. 281.
2. Khalili J. Oral cancer: risk factors, prevention and diagnostic. Experimental Oncology. 2008;30:259–264.
3. Jemal A, Thomas A, Murray T and Thun M. Cancer statistics. Cancer Journal Clinic. 2002;52:23-47.
4. Ananthnarayan R. Immunohematology. In: Text book of microbiology. 3rd ed. New Delhi: Orient 1996. p. 170-1.

5. Scully C, Field J K, Tanzawa H. Genetic aberrations in oral or head and week squamous cell carcinoma. Oral Oncology. 2000;36:311-27.
6. Dabelsteen E, Gao S. ABO blood group antigens in oral cancer. Journal of Dental Research. 2005;84:21-8.
7. Henderson J, Seagrott V and Golgacre M. Ovarian cancer and ABO blood groups.Journal of Epidemiology Common Health. 1993;47:287-289.
8. Onizawa K, Nishihara K, Yamagata K, Yusa H, Yanagawa T and Yoshida H.Fcators associated with diagnostic delay of oral squamous cell carcinoma. Oral Oncology. 2003; 39:781-788.
9. Jain AK. Determination of blood groups. In: Manual of practical Physiology. New Delhi: Arya Publication; 2007.p. 43-45.
10. Cohan J. Statistical power analysis for the behavioral sciences. 2nd ed. Lawerence Erlbaum. London: Associates Publishers; 1988.p. 550
11. Hakomori S. Antigen structure and genetic basis of histo-blood groups A, B and O and their changes associated with human cancer. Biochemical Biophysics Act. 1999;1473: 247-266.
12. Hakomori S. Glycosylation defining cancer malignancy: new wine in an old bottle. Proc National Academic Science. 2002;99:10231-10233.
13. Hakomori S. Structure, organization and function of glycosphingolipids in membrane. Current Opnin Hematology. 2003;10:16-24.
14. Pendu Le J, Marionneau S, Cailleau- Thomas A, Rocher J, Moullac- Vaidye B and Clement M. ABH and Lewis histo- blood group antigens in cancer. Acta Pathologica Microbiologica et Immunologica Scandinavia. 2001;109:9-31.
15. Hakomori S, Koscielak J, Bloch K and Jeanloz R. Immunologic relationship between blood group substances and a fucose- containing glycolipid of adenocarcinoma. Journal of Immunology. 1967;98:31-38.
16. LandsteinerK. Zur Kenntnis der antifermentativen, Lytischen and agglutinierenden Wirkengen des Blutderums und der lymphe.Zbl Bakterial. 1900;27:357-62.
17. Ravn V and Dabelsteen E. Tissue distribution of histo-blood group antigens. Acta Pathologica Microbiologica et Immunologica Scandinavia. 2000;108:1-28.
18. Alexander W. An injury into distribution of the blood groups in patients suffering from malignant disease. British Journal of Experiment Pathology. 1921;2:66.
19. Aird I, Bentall HH, Roberts JA. A relationship between cancer of stomach and the ABO blood groups. British Medical Journal. 1953;1:799-801.
20. Tyagi SP, Pradhan S, Agarwal P. Blood groups in malignant diseases. Journal of Indian Medical Association. 1965;45:645-50.
21. Mittal VP, Gupta S. The study of ABO blood groups in oral cancer. Journal of cancer. 1969;6:34-7.
22. Nayak SK. ABO blood groups in different diseases. Journal of Indian Medical Association. 1971;57:449-52.
23. Baurah BD, Gogoi BC. Blood groups in cancer in Assam, India. Indian Journal of Cancer. 1977;14:6-9.
24. Raaghavan VM, Bailoor DN, Jhansirani P. Incidence of ABO blood groups in oral cancer in South Kanara diatrict. Journal of Indian Dental Associates. 1986;58:305-8.
25. Gao S, Bennett EP, Reibel J, Chen X, Christensen Me, Krogdahl A, Dabelsteen E. Histo blood group ABO antigen in oral potentially malignant lesions and squamous cell carcinoma genotypic and phenotypic characterization. Acta Pathologica Microbiologica et Immunologica Scandinavia. 2004;112:11-20.
26. Hirohashi S. Tumor associated carbohydrate antigen related to blood groupcarbohydrates. Gan To Kagaku Rhyoho. 1986;13:1395-1401.
27. Kurtenkov O, Klaamas K, Miljukhina L. The cancer level of natural anti- Thomsen- Friedenriech antigen (TFA) agglutinins in sera of patients with gastric cancer relaed to ABO (H) blood phenotype. International Journal of Cancer. 1995;60:781-785.
28. Ichikawa D, Handa K, Hakomori S. Histo blood group A/B antigen deletion/ reduction vs. continous expression in human tumor cells as correlated with their malignancy. International Journal of Cancer. 1998;76:284-289.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 26-07-2016; **Published online**: 09-09-2016